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1: Prog Neuropsychopharmacol Biol Psychiatry. 1996 Nov;20(8):1413-25.

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A novel benzodiazepine inverse agonist, S-8510, as a cognitive enhancer.

Kawasaki K, Eigyo M, Ikeda M, Kihara T, Koike K, Matsushita A, Murata S, Shiomi T, Takada S, Yasui M.

Shionogi Research Laboratories, Shionogi & Co., Ltd., Osaka, Japan.

1. Pharmacological actions of a novel benzodiazepine receptor ligand, S-8510 (2-(3-isoxazolyl)-3,6,7,9-tetrahydroimidazo[4,5-d]pyrano++[4,3-b]pyridine monophosphate monohydrate), were examined in in vitro and in vivo studies. 2. S-8510 was characterized as a partial inverse agonist with a modest GABA ratio and low efficacy. 3. S-8510 ameliorated memory impairment induced by cholinergic deficit in the water maze paradigm of Wistar rats. 4. S-8510 augmented LTP of the Schaffer collateral/commissural fiber-CA1 synapses in the hippocampal slice preparations of SD rat. 5. S-8510 increased the extracellular levels of acetylcholine and noradrenaline in the hippocampus of Wistar rat. 6. S-8510 selectively potentiated pentylentetrazol-induced convulsion without affecting minimal electroconvulsive shock- or strychnine-induced convulsion in ddY mice. 7. S-8510 failed to induce any sign of anxiety in the Wistar rat pro-conflict test. 8. S-8510 showed antidepressant-like pharmacological actions in ddY mice. 9. These results suggest that S-8510 can be used as a therapeutic drug for senile dementia, including Alzheimer's disease with little risk for inducing anxiety or convulsion.

PMID: 9004347 [PubMed - indexed for MEDLINE]

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